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Reminder about valproate (Epilim®▼). Readers are reminded of the high teratogenic risk associated with valproate (Epilim®▼); **children exposed in utero to valproate have a 30 to 40% risk of a developmental disorder and a 10% risk of a birth defect.** In 2018, the EU's Pharmacovigilance Risk Assessment Committee (PRAC) recommended important new contraindications, strengthened warnings and other risk minimisation measures to further prevent valproate exposure during pregnancy (***www.ema.europa.eu***). **Valproate-containing medicines are contraindicated in female children and women of childbearing potential (WOCBP),** unless the terms of a special pregnancy prevention programme are followed. The pregnancy prevention programme includes measures to ensure that patients taking valproate are fully aware of the risks and the need to avoid becoming pregnant while taking valproate; full details are in section 4.4 of the Summary of Product Characteristics (SmPC). **If used in female children or WOCBP, valproate must be initiated and supervised by a specialist experienced in the management of epilepsy or bipolar disorder**. Further information is available on the Health Products Regulatory Authority (HPRA) website (***www.hpra.ie***).

Methotrexate – new measures to avoid medication errors! When used in the treatment of inflammatory diseases (e.g. rheumatoid arthritis and psoriasis), methotrexate should only be taken once weekly. However **medication errors with serious consequences (including fatalities) have been reported, when methotrexate intended for once weekly dosing was taken daily**. The EU's PRAC reviewed the evidence and recommended additional measures to reduce the risk of medication errors with methotrexate. Healthcare professionals (HCPs) are advised that:

- Only physicians with expertise in using methotrexate-containing medicines should prescribe them
- Patients who are being prescribed or dispensed methotrexate for inflammatory disease should be given complete and clear dosing instructions on the once-weekly dosing regimen
- It should be checked carefully at every new prescription/dispensing of methotrexate that the patient/carer understands that the medicine must only be used once a week
- The HCP and patient/carer should decide together on which day of the week the patient is to use methotrexate
- The patient should be informed of the signs of overdose and instructed to promptly seek medical advice in case of suspected overdose.

Additional measures to reduce the risk of medication errors with methotrexate include the updating of the product information (including the SmPC and Package Leaflet), production of educational materials for HCPs and patients and the introduction of blister packs for methotrexate. Further information is available on the HPRA (www.hpra.ie) and EMA websites (www.ema.europa.eu).

National Clinical Guideline on psychotropic medication in patients with dementia. The National Clinical Effectiveness Committee recently published a National Clinical Guideline (No 21) on the "*Appropriate prescribing of psychotropic medication for non-cognitive symptoms in people with dementia*". The full guideline and a summary report are available on ***https://www.gov.ie/en/collection/ac0046-appropriate-prescribing-of-psychotropic-medication-for-non-cognitive/***

Patient knowledge of potential interactions between OTC products and apixaban. Direct-acting oral anticoagulants (DOACs) are increasingly used in place of warfarin for the treatment of conditions including non-valvular atrial fibrillation and venous thromboembolism. Although DOACs have less drug and food interactions than warfarin, important potential interactions can occur with DOACs. The majority of patients on DOACs are not monitored as frequently as those on warfarin; this may result in reduced patient education and knowledge about potential interactions between DOACs and OTC medications or dietary supplements. A cross sectional survey of patients on apixaban was undertaken to determine the prevalence of use of OTC products with potentially serious apixaban interactions and to assess patient knowledge of potential interactions ***(J Am Geriatr Soc 2019; DOI: 10.1111/jgs.16193)***. Patients were identified from academic-affiliated outpatient medical practices in California; eligible patients were those who reported taking apixaban for > one month. The survey had a 33% response rate; 791 patients (mean age 71 years) completed the survey, of which 60% were male and 35% of patients had previously been on warfarin. Overall one third of respondents (n=266) reported taking ≥ one OTC product regularly (defined as daily/most days use), which had potentially serious interactions with apixaban; of these **15% reported regular use of OTC aspirin and up to 2% reported regular use of nonsteroidal anti-inflammatory drugs [NSAIDs] (ibuprofen/naproxen)**. An additional 10% reported using aspirin and 29% used NSAIDs on some days or as needed (non-regular). Regular use of dietary supplements (e.g. herbal teas and turmeric) with potential serious interactions with apixaban was reported by 20% of respondents. The study found that respondents with regular use of OTC products were less knowledgeable about potential OTC interactions compared to non-regular users (P<0.01) and that **respondents who had discussed use of OTC products with healthcare professionals were significantly more knowledgeable about potential interactions compared with those who did not (P<0.001)**. Multivariable analyses found that **regular use of aspirin and NSAIDs occurred significantly more often when respondents were less knowledgeable about potential interactions**, while greater health literacy, previous warfarin use and more prescription medicine use was negatively associated with regular aspirin and NSAID use. Limitations of the study include the low response rate and the self-reporting of OTC use, however the study does suggest that patients have limited knowledge of potential serious interactions between OTC products and apixaban. The authors of the study recommend that patients should be educated about the potential harms of using combinations of OTC products and apixaban/other anticoagulants and that adverse events associated with use of this combination should be reported.

Adherence and persistence to oral anticoagulants (OAC). There is a paucity of evidence on patient adherence (taking drugs as prescribed) and persistence (continuation of therapy) for OACs (vitamin K antagonists [VKA] and DOACs) in the same population. A retrospective cohort study using The Health Improvement Network (THIN) database in the UK was undertaken to investigate the adherence and persistence for OACs in individuals with atrial fibrillation (AF) ***(Heart 2020;106:119-126)***. The study included patients ≥18 years diagnosed with first ever non-valvular AF between January 2011 to December 2016 who had a first prescription of VKA/DOAC and who were followed up for ≥90 days. Outcomes were adherence (defined as a proportion of days covered [PDC] >80%) and persistence (defined as persistent until a prescription gap >90 days or switch to an alternate OAC). There were 36,652 patients in the study, (mean age of 74.4 years, 45% were female); VKA (68%), dabigatran (3.5%), rivaroxaban (16%) and apixaban (12%). **Adherence was 52% overall**, and 51%, 66.5%, 63% and 65% for VKA, dabigatran, rivaroxaban and apixaban respectively. There was a reduced likelihood of non-adherence with DOACs compared with VKA. Increasing comorbidity (by CHA_2DS_2VASc), age ≥75 years, diabetes, female gender and anaemia were associated with reduced risk of non-adherence, while hypertension and vascular disease were associated with an increased risk. **One-year persistence was 66% overall**, and 63%, 61%, 72% and 77% for VKA, dabigatran, rivaroxaban and apixaban respectively; persistence reduced over 3 years for all OACs and was highest for apixaban and lowest for VKA and dabigatran. **The results found overall that 40% of patients were both adherent and persistent at 1 year**; this was highest for apixaban (51%) and lowest for VKA (38%). The authors of the study discuss that, as these therapies are usually life long, there is a need for interventions that focus on improving adherence and persistence.

Every effort has been made to ensure that this information is correct and is prepared from the best available resources at our disposal at the time of issue. References are available on request. This ***newsletter is produced by the National Medicines Information Centre, St. James's Hospital (SJH) Dublin 8 and Dept of Therapeutics Trinity College, Trinity Centre, SJH.*** *Tel: Direct Line (01) 473 0589 or 1850 727 727 Email: nmic@stjames.ie*